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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,902	06/19/2006	David Morton	478.1074	1653

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EXAMINER	
KENNEDY, NICOLETTA	
ART UNIT	PAPER NUMBER
1611	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,902	MORTON ET AL.	
	Examiner	Art Unit	
	NICOLETTA KENNEDY	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,11-15 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,7,11-15 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-2, 6-7, 11-15 and 25-29 are currently pending.

Priority

This application, filed March 7, 2006, is a national stage entry of PCT/GB04/03938 filed September 15, 2004, and claims foreign priority to United Kingdom applications 0409133.6 and 0321608.2, filed April 23, 2004 and September 15, 2003 respectively. Applicants have provided certified copies of the United Kingdom applications.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 10, 2011 has been entered.

Withdrawn Rejections

1. The rejection of laims 1 and 11-14 under 35 U.S.C. 102(b) as being anticipated by Staniforth (EP 1 213 012) (pub. June 12, 2002) is withdrawn in view of Applicant's amendments.

New Rejections

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Claim 1-2, 6-7, 11-15 and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has added the limitation "wherein the composition has a fine particle fraction (metered dose) of between 40 and 70%" and cites page 14, lines 22-30. However, this paragraph does not provide support for 40 to 70%. It provides support for at least 40% but not for the upper limit of 70%.

3. The following is a quotation of the appropriate paragraph of 35 U.S.C. 112 that forms the basis for the rejections under this section made in this Office action:

> Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

4. **Claims 6-7, 25 and 27-29 are rejected under 35 U.S.C. 112, fourth paragraph, as failing to further limit claim 1.** Claim 1 contains the limitation "between 40 and 70%." Claims 6-7 claim a particle size (fine particle fraction) of 90% and claims 25 and

27-29 broaden the range of claim 1 by claiming "at least 40%," "at least 50%," "at least 60%" or "at least 70%."

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. **Claims 1, 11-14, 25, and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth (EP 1 213 012) (pub. June 12, 2002) in view of Tarara et al. (US 6,565,885).**

The claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the fine particle fraction is at between 40 and 70%. Fine particle fraction is defined in the instant specification as having a particle size of less than 5 micrometers (p. 14, line 24).

Regarding claims 1, 25 and 27-29, Staniforth teaches improvements in and relating to powders for use in dry powder inhalers (title). The powder is comprised of an active material and an additive material wherein the additive material has been found to give an increased respirable fraction of the active material (abstract). The additive material is leucine and the active material may be heparin (claim 4 and para. 0043). When the additive material is to form a coating on the surface of the particles of active material, the additive may be added to the active material by co-spray drying (para. 0049).

However, Staniforth does not teach a fine particle fraction of 40-70% by weight. Tarara et al. cure this deficiency.

Tarara et al. teach that a dry powder composition for use in a nebulizer for pulmonary delivery has a fine particle fraction of greater than about 40%, 50%, 60% or 70% by weight (column 27, lines 61-64).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have combined the teachings of Staniforth with those of Tarara et al. One of ordinary skill would have been motivated to manipulate the fine particle fraction to control the amount of active medicament delivered per actuation from the nebulizer (Tarara et al., column 27, lines 51-55). MPEP 2144.05 states that "[i]n the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists" quoting *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Regarding claims 6-7, Staniforth claims that at least 95% by weight of the active particles have a particle size between 0.1 and 5 um (claim 27). MPEP 2144.05 states that "[i]n the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists" quoting *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). In the instant case, the claimed range overlaps the range of Staniforth and is therefore prima facie obvious. The size of the particles may be calculated by laser diffraction (para. 0045).

Regarding claims 11-13, Staniforth teaches that the additive material may be added to the active material from a suspension or solution (para. 0049).

Regarding claim 14, Staniforth claims that the powder comprises at least 80% by weight of active material based on the weight of the powder (claim 9).

Response to Arguments

Applicant's arguments filed February 10, 2011 have been fully considered but they are not persuasive. First, Applicant argues that Staniforth prefers a fine particle

fraction of at least 95% by weight of the active particles having a size between 0.1 and 5 micrometers (remarks, p. 10). Next, Applicant argues that Tarara teaches away from formulations like Staniforth because the references have disparate teachings (p. 11). Finally, Applicant argues Tarara individually.

First, the fact that Staniforth has a preferable teaching does not preclude other fine particle fractions, especially in view of the fact that Staniforth teaches larger particle sizes, thus resulting in a lower amount of particles at less than 5 micrometers (see claims 20-21 of Staniforth). Second, Tarara is used to show that the fine particle fraction of a dry powder composition delivered through a nebulizer may be manipulated to change the amount of active agent delivered. Staniforth does not teach away from lower fine particle fractions and neither does Tarara teach away from a high particle fraction. In fact, Tarara teaches that the fine particle fraction may a large range, from 30% and above (column 27, lines 61-64). Finally, lin response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

13. **Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth (EP 1 213 012) (pub. June 12, 2002) in view of Tarara et al. (US 6,565,885) as applied to claims 1, 6-7, 11-14, 25 and 27-29 above, and further in view of Wiedmann et al. (Pharm. Dev. & Tech.).**

The claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the velocity of the droplets at 5 mm from their point of generation is less than 20 m/s.

Staniforth teaches each limitation of claims 1, 6-7, 11-14, 25 and 27-29. However, Staniforth fails to teach the velocity of the droplets. Wiedmann et al. cure this deficiency.

Regarding claim 2, Wiedmann et al. teach an ultrasonic spray system for ultimate use in respiratory drug delivery (abstract). Solvent evaporation is used to remove the solvent (p. 85). The liquid atomization system circumvents several problems with formulation of aerosol solids though it may require an additional step of solvent removal (p. 87). An advantage of the device is the ability to vary doses while maintaining constant particle size (p. 89). The median aerodynamic particle diameters ranged from 1 to over 6 microns (p. 86). Wiedmann et al. explain that the ultrasonic nebulizer is regarded as a soft, low-velocity spray wherein the particles are emitted with an estimated linear velocity of 21cm/s (p. 88). If the initial linear velocity is 21cm/s or 0.21m/s, then the velocity at 5mm from point of generation is less than 20m/s.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have combined the teachings of Staniforth and Tarara et al. with those of Wiedmann et al. One would have been motivated to use an ultrasonic nebulizer to because ultrasonic nebulizers allow smaller particle size, such as that taught by Staniforth, ultimately resulting in deeper penetration of the medicament into the lungs.

Response to Arguments

Applicant's arguments filed February 10, 2011 have been fully considered but they are not persuasive. See Above Response to Arguments. Applicant's arguments with respect to claim 2 have been considered but are moot in view of the new ground(s) of rejection.

14. **Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth (EP 1 213 012) (pub. June 12, 2002) in view of Tarara et al. (US 6,565,885) as applied to claims 1, 6-7, 11-14, 25 and 27-29 above, and further in view of Kuo et al. (US 6,518,239).**

The claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the moisture content of the spray dried particles is adjusted

Staniforth teaches each limitation of claims 1, 6-7, 11-14, 25 and 27-29. However, Staniforth fails to teach that the moisture content of the spray dried particles is adjusted. Kuo et al. cure this deficiency.

Regarding claim 15, Kuo et al. teach a method for increasing dispersibility of an active-agent containing formulation for administration to the lung (abstract). Kuo et al. teach that the spray dried particles may be spray freeze dried (column 12, lines 23-24). Applicants, in the instant specification, state that the moisture content may be adjusted by freeze drying the particles (p. 44).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have combined the teachings of Stanifoth and Tarara et al. with

those of Kuo et al. One of ordinary skill would have been motivated to adjust the moisture content of the composition to maximize the stability of the composition and ease of delivery.

Response to Arguments

Applicant's arguments filed February 10, 2011 have been fully considered but they are not persuasive. See Response to Arguments for the combination of Staniforth and Tarata. Applicant's arguments with respect to claim 15 have been considered but are moot in view of the new ground(s) of rejection.

15. **Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth (EP 1 213 012) (pub. June 12, 2002) in view of Tarara et al. (US 6,565,885) as applied to claims 1, 6-7, 11-14, 25 and 27-29 above, and further in view of Kodas et al. (US 6,051,257).**

The claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the density is greater than 0.1 g/cc.

Staniforth teaches each limitation of claims 1, 6-7, 11-14, 25 and 27-29. However, Staniforth fails to teach the density of the powder or the particular particle size. Kodas et al. cure this deficiency.

Regarding claim 26, Kodas et al. teach that the density of the particles is slightly greater than 1g/cc (column 18, line 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have combined the teachings of Staniforth and Tarara et al. with

those of Kodas et al. One of ordinary skill would have been motivated to do so because Kodas et al. teaches that for dry powder inhalers, it in desirable to have an aerodynamic diameter of about 2 micrometers to control particle distribution, wherein an aerodynamic diameter is defined as a particle which behaves aerodynamically like a spherical particle with a density of 1g/cc (Kodas et al., column 17, lines 60-65).

Response to Arguments

Applicant's arguments filed February 10, 2011 have been fully considered but they are not persuasive. See Response to Arguments for the combination of Staniforth and Tarata. Applicant's arguments with respect to claim 26 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicoletta Kennedy whose telephone number is (571)270-1343. The examiner can normally be reached on Monday through Friday 11:30 to 8:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Gollamudi Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. K./
Examiner, Art Unit 1611

/SHARMILA G. LANDAU/

Supervisory Patent Examiner, Art Unit 1611